Applicants hereby elect the invention identified by the Examiner as Group I, claims 1-16, with traverse.

In the Action, the Examiner also stated that the application contains claims directed to more than one species of the generic invention. Applicants have also been required to elect a single species as follows:

> Species Election I (Groups I and II), applicant must elect one type of lentivirus as recited, for example, in claims 3 and 4;
>
> Species Election II (Group I), applicant must elect one type of selectable marker as recited, for example, in claims 6 and 7 and identify whether or not the election is a positive selectable marker as recited in claim 5;
>
> Species Election III (Group I), applicant must elect one type of mutation target as recited, for example, in claims 11 and 12;
>
> Species Election IV (Group I), applicant must elect one type of cell as recited in claims 15 and 16; and
>
> Species Election V (Group II), applicant must elect one type of selectable medium composition (i.e. bromodeoxyuridine or HAT) as recited in claims 23 and 24.

Applicants hereby make the following species elections, also with traverse:

> Species I: Human immunodeficiency virus type 1 (HIV-1) as one type of lentivirus, readable on claims 3 and 4;
>
> Species II: Hygromycin resistance gene as a positive selectable marker, readable on claims 5-6;
>
> Species III: Thymidine kinase gene as one type of mutation target, readable on claim 11;
>
> Species IV: Dividing cell as one type of cell, readable on claims 14 and15; and
>
> Species V: Bromodeoxyuridine as one type of selectable medium, readable on claims 23-24.

Accordingly, based on the election of Group I and the above species, applicants believe that claims 1-6, 8-11, and 13-16 are readable on this election.

Applicants further note that the Examiner has conceded that at least claims 1, 2, 13, and 14 are generic to the claimed vector and at least claims 17, 18, and 21 are generic to the claimed assay.

Applicants understand that should a generic claim be found to be patentable, applicants may be entitled to the examination of additional species. Applicants also note that with the selection of product claims, should such product claims be found to be allowable, applicants may be entitled to rejoinder of the non-elected process claims.

ARGUMENT

Applicants respectfully traverse the restriction requirement because the claims are linked to form a single inventive concept under PCT Rule 13.1.

As noted by the Examiner, the special technical feature linking vector claims 1-6 with assay claims 17-26 is the lentiviral vector recited in claims 1-16 and used in the assay of claims 17-26. Contrary to the Examiner's assertion, the Manskey et al. article (J. Virol.: 2071-2080, Feb. 2003) in no way teaches or suggests the claimed lentiviral vector.

The lentiviral vector recited in claim 1, which links Groups I and II, is not taught or suggested by the prior art because it comprises a mutational target gene (the *human herpes virus type 1* thymidine kinase gene, HHV-1 *tk*) that allows for **selection** in a mammalian cell line. Manskey et al. do not describe **such a lentiviral vector or assay.** Rather, Mansky et al. describe a lentiviral vector that comprises a *lacZ* mutational target gene that allows **only for screening**. The difference between a capability to select versus a capability to screen in genetic assays is substantial. Mansky et al. describe a system in which identifying mutants can be analogized to finding a needle in a haystack. In contrast, the presently claimed invention may be analogized to identifying the needle in the absence of the haystack.

The difference between a screening assay and selection assay cannot be overemphasized. A screening assay forces the experimenter to examine a large population with a mixture of phenotypes and identify individuals with a particular phenotype. In contrast, a selection assay allows the experimenter to look only at individuals having a particular phenotype. As applied to Mansky et al., the authors manually examined large numbers of cell colonies (tens of thousands) spread among hundreds of plates, and they counted the rare white colonies amid a sea of blue. And, because some mutants exhibited shades of blue, subjectivity and limitations of the eye came into play. This type of screening assay is labor intensive, subjective, and commercially impractical.

In contrast, applicants use a medium selectable for the mutation target gene such as bromodeoxyuridine (BrdU) or HAT (hypoxanthine, aminopterin, and thymidine) to positively select for mutants in a forward or reverse manner, respectively. There is no subjectivity involved because mutants or revertants are the only cells that survive on the plate. The presently claimed invention has promising commercial application because the test can be scaled down and automated into a microtiter plate format, whereas the Mansky et al. screening assay cannot.

It is further important not to mistake the drug resistance markers hygromycin and neomycin with the mutational target genes. Mansky et al. describe a neomycin resistance gene in their lentiviral construct. However, this gene is **not** the mutational target. Likewise, applicants have described a hygromycin resistance gene in the lentiviral construct. However, this gene is also **not** the mutational target. While the neomycin and hygromycin resistance genes allow for selection of cells containing vectors in general, they do **not** allow for selection of cells containing mutant proviruses. Only applicants' assay allows for selection of mutants via BrdU selection for *tk*. The *lacZ* mutational target gene described by Mansky et al. does not allow for selection of mutants; it is limited only to screening.

The presently claimed vector and assay are also unique because they allow for mutants to be propagated and further studied, e.g. sequencing of the mutant proviruses, whereas the Mansky et al. assay does not. Mansky et al. describe a process in which the target cells are stained at the end point with a chemical known as X-gal, which kills all of the cells (Fig. 1B, pg. 2072). From that point, Mansky et al. count the rare white, dead cell colonies amid the sea of dead blue colonies. In contrast, mutant cells in applicants' assay thrive in the selectable medium because they are resistant to it. Consequently, the mutants can be further studied in any was so desired. This is yet another significant distinction over Mansky et al.

The presently claimed invention constitutes a single general inventive concept because the vector and assay work hand-in-hand, with the HIV-1-based vector comprising a selectable mutational target gene and the assay providing a process by which to select for the mutants. For all of the above reasons, applicants submit that the claims relate to a single general inventive concept under PCT Rule 13.1, and the special technical feature linking Groups I and II is not taught or suggested by the prior art.

CONCLUSION

Applicants have elected with traverse Group I and the Species listed above. Applicants believe that claims 1-6, 8-11, and 13-16 are readable on this election. Applicants further have traversed the restriction requirement, and for the reasons discussed above, submit that the claims are linked by a common general inventive concept under PCT Rule 13.1. As such, Applicants believe that the restriction requirement is improper, should be withdrawn, and all of the claims examined.

Respectfully submitted,

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